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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,547	07/07/2000	GUIDO CHRISTIAAN PAESEN	2488-1-001	6622

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Fde Copy

Office Action Summary	Application No. 09/554,547	Applicant(s) PAESEN ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *20-23,29 and 32-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,24-28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-40* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed on 12/15/01 is acknowledged. Claim 40 has been amended. Claims 1-40 are pending in the application.

Priority

2 This application is a PCT/GB98/03397 11/12/1998 which claims priority to Foreign Application United Kingdom 9723945.3 11/12/1997. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

3. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details.

Information Disclosure Statement

4. Information Disclosure Statement filed on 1/8/01 (Paper # 7) is acknowledged and a signed copy is attached to this Office action.

Election

5. Applicant's election of Group VI claims 1-19, 24-28, 30 and 31 drawn to a tissue protein SEQ.ID.NO; 16 with traverse is acknowledged. Applicant claims that the restriction requirement made by the Office under 35 USC 121 (please see page 2, first paragraph of amendment filed on 12/15/01) is not appropriate and requests the Examiner to reconsider the restriction requirement and examine Group XIV, claim 29 along with the claims1-19, 24-28, 30 and 31. The traversal is on the ground(s) that the search and examination of an entire application can be made without serious burden; the Examiner must examine it on the merits, even though it includes claims distinct or independent inventions. However, the Examiner disagrees with the applicant and would like to bring applicant's attention to the restriction requirement under 35U.S.C.371 (Paper # 15). Inventions VI and XIV are not linked by the common generic special

technical feature involving the SEQ.ID.NO 16. Although the applicants above concept may link the two inventions, such concept does not constitute "unity of invention is present" as defined by PCT (37CFR1.475(b-d)) and see PCT Article 17(3)(a) and 1.476(c). Therefore, lack of unity is present (see Paper #15). Therefore, applicant's arguments have not been found persuasive because the application has been filed under 35 U.S.C. 371, Lack of Unity practice was followed as per PCT rule 13.2. PCT rules 13.1 and 13.2 do not provide multiple products and methods within a general inventive concept. Applicant elected first product and a method of use. Accordingly, claims 20-23, 29, 32-40 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-19, 24-28, 30 and 31 (product and method of use, Group VI) are under examination.

The requirement is still deemed proper and is therefore made FINAL.

Applicant is advised to amend the elected claims to recite SEQ.ID.NO: 16 only.

Specification Informalities

6. It is noted that the Abstract of the Disclosure is missing. If applicant desires to include the abstract from PCT/GB98/03397 11/12/1998, the Office would photocopy the abstract from PCT/GB98/03397 and it will be inserted in to the specification.

Claims should begin with "I claim" or "'we claim" or "What is claimed is".

Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 9-10, 12-14, 16, 19, 24-27, 30 and 31are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The product, a tissue protein as claimed, has the same characteristics and utility as that found in nature because the

protein can be obtained from ticks salivary glands. To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations which would distinguish the characteristics and utility of applicant's product as enabled in the specification from the utility of the product as it exists in nature. It is further suggested that such limitation include the terminology " purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source which imparts a distinct utility to the claimed product. For relevant case law see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim Rejections - 35 USC 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-19, 24-28,30 and 31are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified tissue cement protein consisting of an amino acid sequence as shown in SEQ.ID.NO: 16, related to tissue proteins from blood feeding tick R.appendiculatus does not reasonably provide enablement for functional equivalents (see claim 1) or portions (see claim 30) (i.e., mutants, fragments etc) or protein associated with non-self molecules or cement protein attached to a toxin or protein genetically fused to peptides etc. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is not enabled for tissue cement protein functional equivalents or portions or protein associated with non-self molecules or cement protein attached to a toxin or protein genetically fused to peptides etc because it is unclear to one skilled in the art what are these functional equivalents or portions or non-self molecules or toxin or genetically fused peptides embraced by the claims since the specification lacks the parameters (characteristics) used to determine functional equivalents or portions or non-self molecules or toxin or genetically fused peptides. If it is unclear to one skilled in the art what sequences which are embraced by a claim which is based on a specification which lacks the parameters used to determine functional equivalents or portions or protein associated with non-self molecules or cement protein attached to a toxin or protein genetically fused to peptides etc, the specification is non-enabling, since one skilled in the art would not be able to make and use those sequences without undue experimentation.

Further, the specification is totally silent on how these tissue cement functional equivalents or portions or protein associated with non-self molecules or cement protein attached to a toxin or protein genetically fused to peptides are obtained, their characteristics and their use as compositions in therapy or as protective immunogens. Applicant speculates without any evidentiary support that the instant cement protein may be fused to bioactive peptides or toxins for targeting to cancer cells (page 9, lines 25-30 and page 28, lines 5-10) and to isolate interacting proteins from salivary gland extract or cement cone. The skilled artisan would not be able to predictably determine which toxin or which peptide would work to target cancer cells since there are many cancers are prevalent . The specification fails to provide evidence to the claimed product i.e., tissue cement functional equivalents or portions or protein associated with

non-self molecules or cement protein attached to a toxin or protein genetically fused to peptides. Therefore, the claimed product lacks support regarding enablement.

10. Claims 24-27, 30 and 31are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a pharmaceutical composition and vaccine composition (Examiner is viewing as if the claims are drawn to pharmaceutical or vaccine compositions). Enablement of a "pharmaceutical composition" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed pharmaceutical compositions/vaccine is for the treatment of temporary or permanent bonding tissue and control of diseases caused by infections transmitted by arthropod parasites. Thus, the nature of the invention is an immunogenic/therapeutic composition used in the treatment of disease.

Although the specification discloses the claimed composition, and general methods for formulating compositions, there is insufficient guidance which would enable one skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against diseases caused by infections transmitted by arthropod parasites.

At the time the invention was made, pharmaceutical compositions/vaccines comprising the claimed tissue cement protein were not routinely used for the treatment of diseases caused by infections transmitted by arthropod parasites. The specification totally silent and lacks guidance by way of general diseases caused by these ticks (East Coast fever) and working examples which teach an "effective amount" of this composition which would be used for this

purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of unknown diseases caused by the ticks. It is unpredictable whether the claimed pharmaceutical composition, which is disclosed as being immunogenic, would have the added property of generating an immune response sufficient to inhibit infections or in treating infections caused by viruses, bacteria and other pathogens because the specification has not disclosed a link or nexus between the tissue cement and its use in the above infections caused by ticks or pathogens. The cement protein has been shown to develop resistance to the infestation of ticks in rabbits (see Shapiro 1989) not as a vaccine against a disease caused by the tick. Further, it is not routine in the art of immuno therapy to use compositions analogous (tissue cement proteins) to the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

Claim Rejections - 35 USC 112, second paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-19, 24-28, 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague, confusing and it is not clear to the examiner what applicant is claiming. Is this claim drawn to an isolated tissue cement protein comprising an amino acid sequence as

set forth in the SEQ.ID.NO: 16 and said tissue cement protein obtained from blood feeding ectoparasite R.appendiculatus (tick)? Or some thing else?

Claims 2-3 are vague for the recitation of "as hereinbefore defined" What are the metes and bounds of as hereinbefore defined?

Claims 9-14 are vague and indefinite for the recitation of "that is associated with one or more carbohydrate moieties, glycosaminoglycan moieties, peptides, self molecules and non-self molecules." What are the metes and bounds of "that is associated with one or more carbohydrate moieties, glycosaminoglycan moieties, peptides, self molecules and non-self molecules? Does applicant intend to claim fusion proteins or something else?

Claims 5-8 are rejected as being vague and indefinite in the recitation of "derived". Is this composition isolated from blood feeding ectoparasite?

Claims 13 and 14 are rejected as being vague and ambiguous for the recitation of "self molecules and non-self molecules." What are the metes and bound of self molecules and non-self molecules?

Regarding claim 19, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 28 is rejected as being vague for the recitation of "a method of production of the vaccine of claim 27 comprising immunizing an animal--." Is this method drawn to immunizing an animal or some thing else?

Claim 30 recites the limitation " tissue cement portion in line 1. There is insufficient antecedent basis for this limitation in the claim.

13. Claims 24 and 26 provide for the use of the tissue cement protein as pharmaceutical or vaccine component, but, since the claim does not set forth any steps involved in the

method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 24 and 26 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejection - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-8, 17, 24-28, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Shapiro et al 1989, Experimental and Applied Acarology, 7, 33-41.

Shapiro et al 1989 disclose a cement protein adhering to the mouthparts of adult tick R.appendiculatus by immunoblot analysys (figure 1) using ^{125} I label and a method of immunizing rabbits with the cement protein (see abstract, materials and methods on pages 35-36, figure 1, 2 and 3).

Examiner is viewing the claims as having open claim language (i.e., (having). Applicant's use of the open-ended term "having " in claims 1-8, 25, 30 and 31 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified

ingredients, even in major amounts). Therefore, the claims read on native cement protein obtained from ticks which inherently comprises the amino acid sequence as set forth in the SEQ.ID.NO: 16. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art protein and the claimed cement protein are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated cement protein with the cement protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

It is noted that the claims 24-27 and 30-31 are directed to a composition comprising a tissue protein. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey; 152 USPQ 235 (CCPA1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Thus the prior art anticipated the claimed invention.

16. Claims 1, 11,15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Shapiro et al 1986 (J.Parasitology, 72 (3) 454-463).

The claims are drawn to a tissue cement protein expressed in a recombinant form, having the claimed amino acid sequence chemically fused to one or more polypeptides or cross linked to one or more polypeptides.

Shapiro et al disclose antigens from ixodid tick R. appendiculatus. The antigens are isolated from the tick, purified and analyzed via SDS-PAGE. The antigen preparations of

Shapiro (see abstract and pages 455-458) are the same as the claimed tissue protein. Characteristics such as amino acid sequence would be inherent in the preparations of Shapiro et al. Moreover limitations such as chemically linked to other peptides, cross linked to other peptides and expressed in a recombinant form are being viewed as process limitations. Although product-by-process claims are limited and defined by the process, nonetheless, determination of patentability is based on the product itself. The patentability of a product does not depend upon its method of production. If the product in the product-by-process claim is the same as or an obvious variant of the product of the prior art, the claim is unpatentable even though the product was made by a different process. The recitation of process limitations in claims 11, 15 and 16 is not seen as further limiting the claimed product, as it is presumed the equivalent products can be obtained by multiple routes. Where a product-by-process claim is rejected over a prior art product that appears to be identical, although produced by a different process, the burden is upon the applicants to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Thorpe*, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). *In re Marosi*, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). *In re Best*, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). *In re Brown*, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972).

17. Claims 1, 5, 6-10, 12, 13, 24-28, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Dhadialla et al 1985 (G.B 2142334 A).

The claims are drawn to a tissue cement protein from ectoparasite R.appendiculatus expressed in recombinant form, having the recited amino acid sequence, functional equivalents and associated with one or more polypeptides, self-molecules and carbohydrates.

Dhadialla et al disclose immunogenic preparation of antigenic glycoproteins from ixodid tick R. appendiculatus (see abstract, figure VI and page 2, lines 40-65). The antigen

preparations of Dhadialla and method of producing the vaccine are the same as the claimed tissue protein and method. Characteristics such as amino acid sequence, associated with carbohydrate moieties, glycosaminoglycan moieties, one or more peptides and self-molecules would be inherent in the preparations of Dhadialla et al. Moreover limitations such as "use of," vaccine, for use as a vaccine component are being viewed as intended use which carries little patentable weight to the protein. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated cement protein with the cement protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D

3/4/02.

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